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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/028,075	12/21/2001	Nisar Asmed Khan	2183-5223US	1102

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EXAMINER
DUNSTON, JENNIFER ANN

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 04/06/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/028,075	KHAN ET AL.	
	Examiner	Art Unit	
	Jennifer Dunston	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 February 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22* is/are pending in the application.

4a) Of the above claim(s) *6-22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *10/3/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This action is in response to the amendment filed 2/2/2006. Applicants' arguments have been thoroughly reviewed, but are not persuasive for the reasons that follow. Any rejections and objections not reiterated in this action have been withdrawn. **This action is FINAL.**

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Election/Restrictions

Claims 6-22 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 10/28/03.

Information Disclosure Statement

Receipt of an information disclosure statement, filed on 10/3/2005, is acknowledged. The signed and initialed PTO 1449 has been mailed with this action.

Claim Rejections - 35 USC § 103

Claims 1-5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lunardi-Iskandar et al (U.S. Patent No. 5,677,275) in view of Matsushima et al (U.S. Patent No. 5,981,486). This rejection was made in the Office action mailed 9/26/2005 and is reiterated below.

Lunardi-Iskandar et al teach: "Hormone polypeptides that are effective against cancers include the intact hCG and hLH dimers, the beta-subunits of hCG and hLH, and subfragments of the hCG and hLH beta-subunits. ... Among the biologically active subfragments of beta-hCG that are effective against cancer are beta-hCG(109-119). ... So long as the polypeptide or subfragment retains biological activity, it can be used in the claimed cancer treatment methods. To determine whether a particular polypeptide is biologically active, cells that express the hLH-hCG receptor (LH-CG-R) are exposed to the polypeptide fragment being tested, after which the cells are assayed for biological effects that are indicative of hCG or hLH presence." (column 5). Lunardi-Iskandar et al teach contacting cells in animals (mice) with hCG by injecting the mice with hCG (Example 6). The reference teaches that the polypeptide gene product of c-rel was detected in the cells from the mice treated with hCG and not in the cells of mice that had not been treated with hCG (column 13, lines 10-17), which determines the ratio.

Lunardi-Iskandar et al do not specifically teach assaying any specific peptide that is at most 30 amino acids long.

Matsushima et al teach as the size of a peptide becomes shorter, its immunogenicity inside the human body decreases while also being more resistant to decomposition by proteases in the body, thus making it advantageous (column 4).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method of assaying for biological activity of a subfragment of hCG by exposing cells to the subfragment and assaying for biological effects indicative of hCG presence as taught by Lunardi-Iskandar et al by assaying directly for the presence of hCG by injecting mice with hCG detecting the polypeptide gene product of c-rel as taught by Lunardi-Iskandar et

al because Lunardi-Iskandar et al teach that it is within the ordinary skill in the art to test hCG activity by assaying for the presence of c-Rel. Furthermore, it would have been obvious to further modify the assay taught by Lunardi-Iskandar et al by specifically assaying for the smallest subfragments of hCG, such as the smallest subfragments such as beta-hCG(109-119) because Lunardi-Iskandar et al teach that such small hCG fragments have activity, the reference specifically teaches testing subfragments of hCG for activity, and Matsushima et al teach that it is known in the art that as the size of a peptide becomes shorter, its immunogenicity inside the human body decreases while also being more resistant to decomposition by proteases in the body, thus making it advantageous. This would result in some subfragments of at most 30 amino acids being tested because it is taught by Lunardi-Iskandar et al that a hCG fragment of 11 amino acids has activity and thus one would have been motivated to find other small hCG subfragments that also have activity, many of which would be under 30 amino acids in length. The testing of any one of these peptides would make obvious the claimed invention.

One would have been motivated to do so for the expected benefit of making new hCG subfragments that have activity and are minimal in length, that would be effective against cancer, as taught by Lunardi-Iskandar et al, and have decreased immunogenicity and increased resistance to decomposition in the body, as taught by Matsushima et al. Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Response to Arguments

Applicant's arguments filed 2/2/2006 have been fully considered but they are not persuasive. The response essentially asserts that the Examiner has failed to establish and maintain a *prima facie* case of obviousness, because there is no motivation to combine the references cited by the Examiner, and Lunardi-Iskandar and Matsushima, alone or in combination, do not teach or suggest all of the elements of claim 1 or those claims dependent therefrom.

The response asserts that there is no motivation to combine the references. The Examiner stated, "One would have been motivated to do so for the expected benefit of making new hCG subfragments that have activity and are minimal in length, that would be effective against cancer, as taught by Lunardi-Iskandar et al, and have decreased immunogenicity and increased resistance to decomposition in the body, as taught by Matsushima et al." The motivation to combine the references thus comes from some suggestion or teaching of both references applied in the rejection. The response asserts that this is not a sufficient motivation to combine, because Applicants were not attempting to avoid the immunogenicity of the oligopeptide recited in claim 1 and that Applicants teach the use of the peptide in combination with immunogenic adjuvants or as a replacement for the use of adjuvants. In response to applicant's argument that the specification teaches the use of immunogenic adjuvants and high molecular weight carriers during the delivery of the oligopeptide recited in claims 1-5, the fact that applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985). Even if one did not

consider the immunogenicity of the peptide as a factor in combining the references, one would be motivated to use peptides of at most 30 amino acids long in order to obtain peptides with increased resistance to decomposition in the body as taught by Matsushima et al.

The response assets that Lunardi-Iskandar and Matsushima, alone or in combination, do not teach or suggest all the elements of claim 1 or those claims dependent therefore. The response asserts that Matsushima et al discloses "a cell-free investigation of the effects of the peptides of the I-kappaBalpha phosphorylation site on NF-kappaB activation." With regard to the Lunardi-Iskandar reference, the response asserts that the only peptides used by Lunardi-Iskandar et al are the following: 1. Intact native hCG, which is 237 amino acids long, 2. Native β-hCG, which is 145 amino acids long, 3. A fragment of β-hCG, β-hCG$_{(109-145)}$, which is 36 amino acids long; and 4. Native α-hCG, which is 92 amino acids long. The response asserts, "Lunardi-Iskandar does not teach or suggest placing the β-hCG (109-119) in contact with at least one cell and determining the presence of a NF-kappaB/Rel protein in or derived from the at least one cell contacted with the β-hCG (109-119) as recited in claim 1." In fact, Lunardi-Iskandar et al teach that to determine whether a polypeptide fragment is biologically active, one can perform an assay to detect a biological effect that is typical of cells exposed to hCG or hLH, "as described below" (see column 3, lines 48-57). One such test to determine whether a polypeptide has an effect typical of cells exposed to hCG is the elimination of tumor cells by an apoptotic process, which is determined by detecting the presence of c-rel as taught in Example 7 of Lunardi-Iskandar. Although Lunardi-Iskandar et al do not exemplify the use of the 36 amino acid β-hCG (109-119) peptide in this particular assay, Lunardi-Iskandar et al teach that any fragment may be tested in the disclosed assays to determine whether it has biological activity.

Furthermore, Lunardi-Iskandar et al specifically teach the production of fragments fewer than about 50 amino acids (e.g. column 4, lines 15-24). Moreover, Lunardi-Iskandar et al teach the use of commercially available hCG such as Pregnyl™ (e.g. paragraph bridging columns 3-4). It is known in the art that Pregnyl™ contains short peptides less than 30 amino acids (peptides < 1 kDa, WO 99/59617; e.g. page 36, lines 18-36; Figure 98). Thus, as stated on page 4 of the prior Office action, Lunardi-Iskandar teach all of the claim limitations, except Lunardi-Iskandar et al do not specifically teach assaying a peptide that is at most 30 amino acids long. This deficiency in Lunardi-Iskandar is met in view of the teachings of Matsushima et al. One would only have to remove 6 amino acids from the β-hCG (109-119) peptide of Lunardi-Iskandar et al to meet each of the claim limitations. In view of the teachings of Lunardi-Iskandar et al and Matsushima, it would have been obvious to one of ordinary skill in the art at the time the invention was made to include the use of peptides of at most 30 amino acids in the method of Lunardi-Iskandar et al.

For these reasons, and the reasons made of record in the previous office actions, the rejection is maintained.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after

the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Dunston whose telephone number is 571-272-2916. The examiner can normally be reached on M-F, 9 am to 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel can be reached at 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR, http://pair-direct.uspto.gov) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Jennifer Dunston, Ph.D.
Examiner
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PRIMARY EXAMINER